UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,381	08/15/2006	Annaliesa S. Anderson	21490YP	5673

210 7590 06/12/2008

MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	PAPER NUMBER
1645	
MAIL DATE	DELIVERY MODE
06/12/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,381	ANDERSON ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *8-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08/15/06* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *091107*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Preliminary Amendments

1) Acknowledgment is made Applicants' preliminary amendments filed 08/15/06, 09/11/07, 12/10/07 and 03/04/08.

Election

2) Acknowledgment is made Applicants' election filed 09/17/08 in response to the written lack of unity mailed 08/14/07. Applicants have elected, with traverse, invention I, claims 1-7, drawn to a polypeptide immunogen. Applicants' traversal is on the grounds that the current amendment to claim 1 indicates that the polypeptide of claim 1 consists of an amino acid sequence 'with up to 26 amino acid alterations from SEQ ID NO: 1'. Applicants state that WO 03/011899 does not appear to describe a polypeptide claimed in claim 1. Applicants further state that their arguments concerning the restriction requirement are not arguments concerning the patentability of one claim or group of claims in light of another claim or group of claims, but are directed to the Office's basis of unity of invention.

Applicants' arguments have been carefully considered, but are not persuasive. The lack of unity set forth in the Office Action mailed 08/14/07 was based on the claims as originally filed. The base claims have now been amended. Even the polypeptide immunogen of the amended claim 1, for example, does not define over the prior art. See the art rejections set forth below. Therefore, the written lack of unity set forth in the Office Action mailed 08/14/07 is proper, is maintained, and is hereby made FINAL.

Status of Claims

3) Claims 3, 6, 8, 10 and 15 have been amended via the amendment filed 08/15/06.
Claims 1, 2, 5 and 15 have been amended via the amendment filed 12/10/07.
New claims 16-20 have been added via the amendment filed 12/10/07.

Claims 1, 2, 5 and 15 have been amended via the amendment filed 03/04/08.

Claims 8-18 have been withdrawn from consideration as being directed to a non-elected species. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

Claims 1-20 are pending.

Claims 1-7, 19 and 20 are under examination.

Information Disclosure Statement

4) Acknowledgment is made of Applicants' information disclosure statement filed 09/11/07. The information referred to therein has been considered and a signed copy of the same is attached to this Office Action.

Sequence Listing

5) Acknowledgment is made of Applicants' sequence listing which has been entered on 08/22/0/06.

Priority

6) This application is a national stage application filed under 35 U.S.C § 371 of PCT/US05/04431, filed 02/14/05, which claims the benefit of the provisional application 60/545,447, filed 02/18/04.

Objection(s) to Specification

7) The instant specification is objected to for the following reasons:

(a) The amino acid sequence, LPXTG, depicted on pages 2, 5 and 16 of the instant specification is not identified by a specific SEQ ID number as required under 37 C.F.R 1.821 through 1.825. Any sequences recited in the instant specification, which are encompassed by the definitions for nucleotide and/or amino acid sequences as set forth in 37 C.F.R. 1.821(a)(1) and (a)(2) must comply with the requirements of 37 C.F.R 1.821 through 1.825. Note that branched sequences are specifically excluded from this definition.

APPLICANT MUST COMPLY WITH THE SEQUENCE RULES WITHIN THE SAME TIME PERIOD AS IS GIVEN FOR RESPONSE TO THIS ACTION, 37 C.F.R 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R 1.821(g).

(b) The use of trademark recitations in the instant specification has been noted. For example, see 'Coomassie' on pages 5 and 18; and 'Coomassie Blue' on page 16 of the instant specification. The trademark recitations should be capitalized wherever they appear. See M.P.E.P 608.01(V) and Appendix l. Although the use of trademarks is permissible in patent

applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification to make similar corrections to trademark recitations, wherever such recitations appear.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (Written Description)

8) The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9) Claims 1-7, 19 and 20 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1 and 2 are drawn to a genus of polypeptide immunogen variants consisting of an amino acid sequence from SEQ ID NO: 1 wherein the amino acid sequence has up to 26 or 20 amino acid alterations and wherein the polypeptide immunogen provides protective immunity against *S. aureus*. Claim 5, as amended, is drawn to an immunogen comprising a polypeptide consisting of an amino acid sequence with up to 26 amino acid alterations from SEQ ID NO: 1, wherein said polypeptide provides protective immunity against *S. aureus* and has one or more additional regions or moieties covalently joined to said polypeptide at the carboxyl terminus or amino terminus, wherein each region or moiety is independently selected from a region or moiety having at least one of the following properties: enhances the immune response, facilitates purification, or facilitates polypeptide stability, and said additional region or moiety is different from a sai-1 region. Claims 6 and 7 are drawn to a composition comprising the immunogen of claim 5. The limitation 'an amino acid sequence ….. from SEQ ID NO: 1' encompasses any sequence of any length from within SEQ ID NO: 1, including a portion of SEQ ID NO: 1 as long as it is immunogenic, has 0-26 amino acid alterations, and provides protective immunity against *S. aureus*. The limitation '*S. aureus*' encompasses homologous or heterologous strains of *S. aureus*, coagulase-positive and coagulase-negative *S. aureus*; multiple drug-resistant and

methicillin-resistant strains of *S. aureus* (MRSA), various phage types of *S. aureus*, and various other serotypes including non-typeable *S. aureus*. For instance, von Eiff *et al.* (*Diagn. Microbiol. Infect. Dis.* 58: 297-302, 2007) teach the prevalence of clinical isolates of *S. aureus* as various *spa* serotypes and capsular serotypes. See abstract of von Eiff *et al.* von Eiff *et al.* characterizes *S. aureus* to be one of the most 'feared' microorganisms because of its ability to cause serious and fatal infections. Although the polypeptide immunogen of the base claim 1 'consists of' an amino acid sequence with up to 26 amino acid alterations from SEQ ID NO: 1, the polypeptide of claim 3 'consists essentially of' amino acids 3-260 of SEQ ID NO: 1 or 3-264 of SEQ ID NO: 2. The limitation 'consisting essentially of' defined on page 7 of the specification allows the inclusion of additional amino acids at the carboxyl or amino terminus of the recited SEQ ID NO: 1, which does not exclude a sai-1 region. The polypeptide of the dependent claim 20 is at least 99% identical to SEQ ID NO: 1 and is *required* to provide protective immunity against homologous or heterologous *S. aureus*. Except for the polypeptide immunogen of claims 19 and 20, the polypeptide immunogen claimed in the rest of the claims is not required to be purified, and not even required to be isolated. Thus, the claims are drawn to a vast genus of polypeptide immunogen variants or immunogens comprising polypeptide variants that have up to 26 or 20 amino acid alterations from SEQ ID NO: 1, or polypeptide variants that are at least 99% identical to SEQ ID NO: 1, each having the ability to provide protective immunity against *S. aureus*. Any amino acids in any number up to 20 or 26 may be substituted along the length of SEQ ID NO: 1 as long as the polypeptide consists of the sequence as recited, or as long as there is 99% or greater sequence identity to SEQ ID NO: 1. The specification intends at least prophylactic applications for the claimed polypeptide or the immunogen variant.

The *Written Description Guidelines* state:

> There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between the structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function.

The written description requirement can be met by describing the claimed subject matter to a person skilled in the art by describing sufficiently detailed, relevant identifying characteristics such as functional characteristics, and correlating those functional characteristics with a disclosed structure. See *Enzo Biochem v. Gen-Probe,* 323 F.3d 956, 964, 967, 968 (Fed. Cir. 2002).

Sufficient description to show possession of a genus may be achieved by means of recitation of a representative number of polypeptides, defined by amino acid sequences falling within the scope of the genus, or recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. Possession may *not* be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. See *University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895.

In the instant application, Applicants have shown possession of one protective polypeptide immunogen species, i.e., the amino acid sequence of SEQ ID NO: 3, which has been depicted in Figure 3. Figure 7B shows that a vaccine comprising SEQ ID NO: 3 in aluminum hydroxyphosphate adjuvant protected 50% of the immunized mice against an intravenous challenge with one strain of *S. aureus* of unspecified serotype, Spa type, capsular type, or phage type. See page 18. This 50% survival among immunized mice is characterized in the instant specification as protection. SEQ ID NO: 3 comprises SEQ ID NO: 1 plus 20 extra amino acid residues at the N-terminus of SEQ ID NO: 1. However, the description of a single protective polypeptide immunogen species within a claimed genus may not be sufficient to support the patentability of the genus under 35 U.S.C § 112, first paragraph. See *University of California v. Eli Lilly & Co.*, 119 F.3d 15559, 1567, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997). The specification does not disclose any polypeptide immunogen variants in which an amino acid sequence consisting of SEQ ID NO: 1 is varied to contain up to 20 or 26 amino acid alterations, or is at least 99% identical to said SEQ ID NO: 1, wherein the polypeptide variants have the recited requisite protection function. The instant specification does not disclose which 1-20 or 1-26 amino acid residues within SEQ ID NO: 1, or which 1% of amino acid residues within SEQ ID NO: 1, should be altered within the polypeptide species of SEQ ID NO: 1 in order to maintain the required biological function, i.e., the capacity to provide protective immunity against homologous or heterologous strain or serotype of *S. aureus*. No other amino acid sequences of isolated or non-isolated polypeptide variants having 1-20 or 1-26 amino acid residues within SEQ ID NO: 1, or 1% of amino acid residues within SEQ ID NO: 1 altered, wherein the isolated polypeptide is *capable of providing protective immunity against homologous or heterologous strain* or *serotype*

of S. aureus. There is a lack of description of the structure of a representative number of isolated or non-isolated, purified or non-purified polypeptide immunogen variants in which an amino acid sequence consisting of SEQ ID NO: 1 is varied to contain up to 1-20 or 1-26 amino acid alterations, or is at least 1% non-identical to said SEQ ID NO: 1, wherein the polypeptide has the requisite function, i.e., *the capacity to provide protective immunity against homologous or heterologous strain* or *serotype of S. aureus.* It should be noted that written description requires more than a mere statement that something is a part of the invention. Applicants have not described what domains, contiguous or discontiguous antigenic determinants, or conformational or non-conformational epitopes of the claimed polypeptide immunogen variant are correlated with the required capacity to provide protective immunity against homologous or heterologous strain or serotype of *S. aureus.* Note that the limitation 'polypeptide … consisting of an amino acid sequence with up to … amino acid alterations from SEQ ID NO: 1' encompasses an isolated and non-isolated, denatured and non-denatured, purified or non-purified, and properly folded and improperly folded SEQ ID NO: 1 having said alterations and the one as present on or in homologous or heterologous *S. aureus* cells.

With respect to the written description requirement, while 'examples explicitly covering the full scope of the claim language' typically will not be required, a sufficient number of representative species must be included 'to demonstrate that the patentee possesses the full scope of the [claimed] invention'. *Lizardtech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345, 76 USPQ2d 1724, 1732 (Fed. Cir. 2005). In the instant case, Applicants' specification does not contain a written description sufficient to show they had possession of the full scope of their claimed invention at the time the application was filed. The instant specification mentions of 'a polypeptide at least 85% identical to SEQ ID NO: 1 containing up to 26 amino acid alterations from SEQ ID NO: 1 … at least … 99% identical to SEQ ID NO: 1' with or without the sai-1 region. The 'alterations' are said to include addition, deletion, or substitution. See for example page 7 of the specification. The specification in the last paragraph of page 7 describes that substituting amino acids have similar properties such as amino acid size, charge, polarity, and hydrophobicity. However, the specification does not disclose a correlation between the function (i.e., capacity to provide protective immunity against homologous or heterologous strain or

serotype of *S. aureus*) and the precise structure or epitope(s) responsible for providing protective immunity against homologous or heterologous strain or serotype of *S. aureus*, other than SEQ ID NO: 3, such that a skilled artisan would have known what alterations including deletions, substitutions, or variations could be made of the large number of alterations currently encompassed within the scope of the instant claims without losing the protective function. Clearly, Applicants did not describe the invention of the instant claims sufficiently to show that they had possession of the claimed genus of polypeptide immunogen variants. See e.g., *Noelle v. Lederman*, 355 F.3d 1343, 1348, 69 USPQ2d 1508, 1513 (Fed. Cir. 2004) ('invention is, for purposes of the written description inquiry, *whatever is now claimed*'). Applicants should note that written description requires more than a mere statement that something is a part of the invention and a reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The specification intends prophylactic (vaccine) and therapeutic applications for the claimed polypeptide immunogen variant. See page 12 of the specification. Whether or not the polypeptide of SEQ ID NO: 1 is *S. aureus* capsular type-specific, *spa* serotype-specific, phage type-specific, is not known. If serotype-specific, *spa* serotype-specific, or phage type-specific, the antigenic determinants within SEQ ID NO: 1 would have variant structure. As known in the art of immunology, an epitope or antigenic determinant can be linear, or conformational or discontinuous, and it interacts with its corresponding antibody based on the three dimensional structure of both molecules and the fit between the molecules. See page 46 of Cruse *et al.*, *Illustrated Dictionary of Immunology*, 2nd Edn., CRC Press, 2003. The specification does not adequately describe or identify the linear or conformational epitopes, generically *S. aureus*-specific, or *S. aureus* serotype-specific, non-serotype-specific or *S. aureus* strain-specific, within SEQ ID NO: 1 or within an amino acid sequence with up to 20 or 26 amino acid alterations from SEQ ID NO: 1, or within an amino acid sequence at least 99% identical to SEQ ID NO: 1. This description is important because a change of even a single amino acid residue can alter the folding of a polypeptide such that the antibody-binding region no longer recognizes the polypeptide. See right column on page 33 of Colman PM. *Research Immunol.* 145: 33-36, 1994. The specification in the last paragraph of page 7 describes that substituting amino acids have

similar properties such as amino acid size, charge, polarity, and hydrophobicity. However, it is recognized in the art that even a very conservative substitution may abolish binding. See first full paragraph on page 35 of Colman. Colman taught that binding interactions could be considered less tolerant because the changes involved occur in what might be called the active site. See third full paragraph on page 35 of Colman.

The antigenic epitopes of bacterial polypeptides are known to be serogroup-specific, serotype-specific, immunotype-specific, subtype-specific, *spa* type-specific, capsular type-specific, or strain-specific. As set forth above, the antigenic epitopes can be linear or non-linear, contiguous or discontiguous. Discontiguous epitopes are formed from different regions of the primary sequence brought together by proper protein folding. Antibodies binding to conformational epitopes bind only to proteins folded into their proper native form. See page 166 of Cruse *et al. Illustrated Dictionary of Immunology*, 2nd Edn., CRC Press, 2003. Linear epitopes are generally not found on the surface of a folded polypeptide and are available to antibodies only upon denaturation of a polypeptide. See page 382 of Cruse *et al.* Since the instant invention contemplates protective, prophylactic (vaccine), or therapeutic applications for the claimed polypeptide immunogen varaint, the claimed product has to provide protective immunity against homologous or heterologous strain or serotype of *S. aureus*. Although a microbial polypeptide having up to 20 or 26 amino acid alterations, or at least 1% non-identity with the native polypeptide is expected in the art to generally induce some antibodies, the capacity of such antibodies to provide protective immunity against homologous or heterologous strain or serotype of *S. aureus* is not predictable. The art reflects unpredictability as to which amino acids in a specific protein can be varied, i.e., replaced or added, without adversely affecting the functional properties of that specific protein. In other words, the retention of the immunospecificity following one or more amino acid substitutions within a bacterial polypeptide or within an at least 10 amino acid-long fragment thereof is not predictable. For instance, McGuinnes *et al.* (*Mol. Microbiol.* 7: 505-514, Feb 1993) taught that "[a] single amino acid change within an epitope, or an amino acid deletion outside an epitope, were both associated with loss of subtype specificity resulting from a change in the predicted conformation at the apex of the loop structure" in case of a meningococcal polypeptide (see abstract). Similarly, McGuinnes *et al.* (*Lancet* 337: 514-517,

March 1991) taught that a point mutation generating a single amino acid change in a P1.16-specific epitope in the VR2 region of the *porA* gene of a strain of *Neisseria meningitidis* of subtype P1.7,16 resulted in "striking changes in the structural and immunological properties of the class 1 protein" of this isolate. See abstract and page 514 of McGuinnes *et al.* Thus, the state of the art at the time of the invention documents the unpredictability in obtaining a functional variant of a microbial polypeptide that retains its specific immunological binding function(s). In the instant case, the polypeptide of SEQ ID NO: 1 is asserted to be a novel polypeptide of *S. aureus*. However, what is claimed is not an isolated polypeptide consisting of SE ID NO: 1. Applicants are claiming a vast genus of polypeptide immunogen variants having up to 20 or 26 amino acid alterations from SEQ ID NO: 1, or having at least 99% identity to SEQ ID NO: 1 wherein the polypeptide immunogen variants are capable of providing protective immunity against homologous or heterologous strain or serotype of *S. aureus*. However, Applicants have not described which domains or regions of the claimed polypeptide immunogen variants are correlated with the required capacity to provide protective immunity against homologous or heterologous strain or serotype of *S. aureus*. Applicants have not described which of SEQ ID NO: 1's amino acids can be varied such that the polypeptide immunogen variant still maintains the capacity to provide protective immunity against homologous or heterologous strain or serotype of *S. aureus*. Without a convincing correlation between structure and function, the claims do little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *Ex parte Kubin*, 83 USPQ2d 1410 (Bd. Pat. Appl. & Int. 2007) citing *Eli Lilly*, 119 F.3d at 1568, 43 USPQ at 1406 ('definition by function ..... does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is'). The instant claims are viewed as not meeting the written description provision of 35 U.S.C. § 112, first paragraph.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

10) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

11) Claims 1-7, 19 and 20 are rejected under 35 U.S.C § 112, second paragraph, as being

indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 1 is indefinite because it has improper antecedent basis in the limitation: 'said polypeptide' (see line 3). The earlier recitation in the claim is of a 'polypeptide immunogen', but not of a 'polypeptide'. For proper antecedent basis, it is suggested that Applicants replace the above-identified limitation with the limitation --said polypeptide immunogen--.

(b) Claim 1 is indefinite because it is incorrect in the limitation: 'An polypeptide' as opposed to the limitation --A polypeptide--.

(c) Claims 2-4, 19 and 20 are indefinite because these claims have improper antecedent basis in the limitation: 'The polypeptide of claim …' (see line 1). Claims 2-4, 19 and 20 depend directly or indirectly from claim 1, which is drawn to a 'polypeptide immunogen', but not to a 'polypeptide'. For proper antecedent basis, it is suggested that Applicants replace the above-identified limitation with the limitation --The polypeptide immunogen of claim …--.

(d) Claim 5 is indefinite in the limitation: 'additional region or moiety … different from a sai-1 region' because it is unclear what precise structure is encompassed in this additional region or moiety. Does a single amino acid residue qualify as an additional region or moiety different from a sai-1 region?

(e) In claim 5, for proper antecedent basis, it is suggested that Applicants replace the limitation 'amino terminus' with the limitation --the amino terminus--.

(f) Claims 2-7, 19 and 20, which depend from claim 1 or 5, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

12) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless –
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13) Claims 1, 2, 4 and 19 are rejected under 35 U.S.C. § 102(b) as being anticipated by Foster *et al.* (WO 2003011899 A2 – Applicants' IDS) ('899).

The limitation 'an amino acid sequence ….. from SEQ ID NO: 1' encompasses any sequence of any length from within SEQ ID NO: 1, including any portion of SEQ ID NO: 1 as long as it is immunogenic, has 0-26 amino acid alterations, and provides protective immunity against *S. aureus*.

Foster *et al*. ('899) disclosed an antigenic protein from *Staphylococcus aureus* or its part for use as a vaccine in immunizing an animal against a disease or condition caused by *Staphylococcus aureus*. The protein consists of the amino acid sequence ADA89581 that is 246 amino acids in length. See claims 4, 7 and 10; and pages 10 and 146. The prior art protein thus has 14 amino acids deleted therefrom and therefore meets the limitation 'polypeptide …. consisting of an amino acid sequence with up to 26 or 20 amino acid alterations from SEQ ID NO: 1. The prior art protein does not contain an additional region or moiety from a sai-1 region.

```
 Query Match             73.9%;  Score 989;  DB 6;  Length 246;
  Best Local Similarity   100.0%;  Pred. No. 1.1e-72;
  Matches  188;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 TQVSQATSQPINFQVQKDGSSEKSHMDDYMQHPGKVIKQNNKYYFQTVLNNASFWKEYKF 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         59 TQVSQATSQPINFQVQKDGSSEKSHMDDYMQHPGKVIKQNNKYYFQTVLNNASFWKEYKF 118

Qy         61 YNANNQELATTVVNDNKKADTRTINVAVEPGYKSLTTKVHIVVPQINYNHRYTTHLEFEK 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        119 YNANNQELATTVVNDNKKADTRTINVAVEPGYKSLTTKVHIVVPQINYNHRYTTHLEFEK 178

Qy        121 AIPTLADAAKPNNVKPVQPKPAQPKTPTEQTKPVQPKVEKVKPTVTTTSKVEDNHSTKVV 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        179 AIPTLADAAKPNNVKPVQPKPAQPKTPTEQTKPVQPKVEKVKPTVTTTSKVEDNHSTKVV 238

Qy        181 STDTTKDQ 188
              ||||||||
Db        239 STDTTKDQ 246
```

The prior art 246 amino acid-long polypeptide consisting of an amino acid sequence from SEQ ID NO: 1 is long enough to be immunogenic. The prior art polypeptide is identical in structure to the instantly claimed polypeptide immunogen, and therefore necessarily possesses all the functions of the instantly claimed polypeptide immunogen including the capacity to provide protective immunity against *Staphylococcus aureus.*

Claims 1, 2, 4 and 19 are anticipated by Foster *et al*. ('899).

14) Claims 1, 2, 4 and 19 are rejected under 35 U.S.C. § 102(b) as being anticipated by Foster *et al*. (WO 200198499 A1– Applicants' IDS) ('499).

The limitation 'an amino acid sequence ….. from SEQ ID NO: 1' encompasses any sequence of any length from within SEQ ID NO: 1, including any portion of SEQ ID NO: 1 as long as it is immunogenic, has 0-26 amino acid alterations, and provides protective immunity against *S. aureus*.

Foster *et al*. ('499) disclosed a purified antigenic polypeptide expressed by pathogenic *Staphylococcus aureus* comprising the amino acid sequence AAU75475 that is 106 amino acids in length and a vaccine comprising the same. The vaccine is used for immunizing an animal against pathogenic *Staphylococcus aureus* and for treating *Staphylococcus aureus*-associated infections. See claim 18; page 10; and SEQ ID NO: 14 on page 20 of the 'Sequence Listing' of Foster *et al*. ('499).

```
Query Match             27.0%;  Score 361;  DB 5;  Length 106;
  Best Local Similarity   100.0%;  Pred. No. 1e-21;
  Matches   72;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0.

Qy        187 DQTKTQTAHTVKTAQTAQEQNKVQTPVKDVATAKSESNNQAVSDNKSQQTNKVTKHNETP 246
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 DQTKTQTAHTVKTAQTAQEQNKVQTPVKDVATAKSESNNQAVSDNKSQQTNKVTKHNETP 60

Qy        247 KQASKAKELPKT 258
              ||||||||||||
Db         61 KQASKAKELPKT 72
```

The 106 amino acid-long polypeptide of the prior art consisting of an amino acid sequence from SEQ ID NO: 1 is long enough to be immunogenic. The prior art polypeptide is identical in structure to the instantly claimed polypeptide immunogen, and therefore necessarily possesses all the functions of the instantly claimed polypeptide immunogen including the capacity to provide protective immunity against *Staphylococcus aureus.*

Claims 1, 2, 4 and 19 are anticipated by Foster *et al*. ('499).

15) Claims 1-3, 19 and 20 are rejected under 35 U.S.C § 102(b) as being anticipated by Foster *et al*. (WO 2003011899 A2 – Applicants' IDS) ('899).

The polypeptide immunogen 'consisting of an amino acid sequence' of claim 1 or claim 2 has no length limit and is not required to be SEQ ID NO: 1, but is required to have up to 26 or up to 20 amino acid alterations from SEQ ID NO: 1.

It is noted that the instant specification defines the limitation 'consisting essentially of' in the dependent claim 3 as including additional amino acids at the carboxyl or the amino terminus.

Therefore, the limitation 'consisting essentially of' is being interpreted in this rejection as equivalent to the open claim language 'comprising'.

Foster *et al.* ('899) disclosed a purified polypeptide immunogen of MW 38,745 comprising an amino acid sequence at least 99% identical to SEQ ID NO: 1 (ADA89548) and which elicits opsonic (i.e., protective) antibodies. A vaccine composition comprising the polypeptide and a carrier and/or an adjuvant is taught. The polypeptide further comprises a secretion signal to facilitate purification. See Table 8 on page 140; claims 4-12; and pages 10-16. The prior art polypeptide immunogen thus consists essentially of 3-260 amino acid of SEQ ID NO: 1 and additional amino acids at its carboxyl or amino terminus. See the sequence alignment report below:

```
  Query Match             99.2%;  Score 1339;  DB 6;  Length 350;
  Best Local Similarity   100.0%;  Pred. No. 4.4e-101;
  Matches  258;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0.

Qy          3 TQVSQATSQPINFQVQKDGSSEKSHMDDYMQHPGKVIKQNNKYYFQTVLNNASFWKEYKF 62
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         59 TQVSQATSQPINFQVQKDGSSEKSHMDDYMQHPGKVIKQNNKYYFQTVLNNASFWKEYKF 118

Qy         63 YNANNQELATTVVNDNKKADTRTINVAVEPGYKSLTTKVHIVVPQINYNHRYTTHLEFEK 122
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        119 YNANNQELATTVVNDNKKADTRTINVAVEPGYKSLTTKVHIVVPQINYNHRYTTHLEFEK 178

Qy        123 AIPTLADAAKPNNVKPVQPKPAQPKTPTEQTKPVQPKVEKVKPTVTTTSKVEDNHSTKVV 182
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        179 AIPTLADAAKPNNVKPVQPKPAQPKTPTEQTKPVQPKVEKVKPTVTTTSKVEDNHSTKVV 238

Qy        183 STDTTKDQTKTQTAHTVKTAQTAQEQNKVQTPVKDVATAKSESNNQAVSDNKSQQTNKVT 242
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        239 STDTTKDQTKTQTAHTVKTAQTAQEQNKVQTPVKDVATAKSESNNQAVSDNKSQQTNKVT 298

Qy        243 KHNETPKQASKAKELPKT 260
              ||||||||||||||||||
Db        299 KHNETPKQASKAKELPKT 316
```

Claims 1-3, 19 and 20 are anticipated by Foster *et al.* ('899).

Rejection(s) under 35 U.S.C. § 103

16) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person. having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

17) Claims 5-7 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Foster *et al.* (WO 200198499 A1 - Applicants' IDS) ('899) or Foster *et al.* (WO 200198499 A1 - Applicants' IDS) ('499) and further in view of Devi *et al.* (US 6,855,807, filed 6/16/1999).

The reference of Devi *et al.* is applied in this rejection because it qualifies as prior art under subsection (e) of 35 U.S.C. § 102 and accordingly is not disqualified under U.S.C. 103(a).

The teachings of Foster *et al.* ('899) or Foster *et al.* ('499) are explained above which do not teach the presence of one or more additional regions or moieties covalently joined to their polypeptide immunogen that is 246 or 106 amino acid-long at the carboxyl terminus or amino terminus, wherein said additional moiety or region is different from sia-1 region.

However, it was routine and conventional in the art at the time of the invention to add an additional sequence tag such as a polyhistidine tag (i.e., a moiety or region is different from sia-1 region) to an art-known polypeptide or protein amino acid sequence to facilitate purification of the polypeptide or the protein. For example, see second full paragraph in column 9 of Devi *et al.*

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to covalently attach an additional amino acid sequence tag such as Devi's polyhistidine tag to Foster's ('899 or '499) staphylococcal polypeptide sequence to produce the instant invention with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of further purifying Foster's ('899 or '499) staphylococcal polypeptide sequence since highly purified microbial polypeptides are highly desired in the art of microbial vaccines.

Claims 5-7 are *prima facie* obvious over the prior art of record.

Remarks

18) Claims 1-7, 19 and 20 stand rejected.

19) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

20) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

21) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Shanon Foley, can be reached on (571) 272-0898.

/S. Devi/
S. Devi, Ph.D.
Primary Examiner
AU 1645

June, 2008